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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/626,891	07/24/2003	Dongmei Xu	07678/078003	2555

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EXAMINER	
ZHENG, LI	
ART UNIT	**PAPER NUMBER**
1638	

DATE MAILED: 06/23/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/626,891	XU ET AL.	
	Examiner	Art Unit	
	Li Zheng	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 April 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-19* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *7/23/2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *7232003/4072006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Examination of this application has been transferred to Li Zheng, Art Unit 1638.

Election/Restrictions

2. Applicant's election with traverse of Group I, claims1-17, in the reply filed on 4/07/2006 is acknowledged. Applicants also elected nucleotides 1 to 332 of SEQ ID NO:1. Non-elected subject matter should be removed from the claims. The traversal is on the ground(s) that the search and examination of all three sequences in claim 3 do not present an undue burden. The examiner maintains that the search and examining of all three sequences is undue, as each group requires searching for different construct components and analysis of unrelated literatures. Applicants are reminded that nucleotide sequences encoding different proteins are structurally distinct chemical compounds and are unrelated to one another. These sequences are thus deemed to normally constitute **independent and distinct** inventions within the meaning of 35 U.S.C. 121. Absent evidence to the contrary, each such nucleotide sequence is presumed to represent an independent and distinct invention, subject to a restriction requirement pursuant to 35 U.S.C. 121 and 37 CFR 1.141 et seq.

However, during the examination, it was determined that it would not be an undue burden to search and examine the invention groups I-III together. Groups I-III, claims 1-19, are therefore rejoined. Applicants are advised that since the restrictions

between Groups I-III are withdrawn, if any claim(s) that include(s) the limitation of the examined claims is/are presented in a continuation or divisional application, the claim of the application may be subject to a provisional statutory and/or nonstatutory double patenting rejection over the claims of the instant application. Where a restriction requirement is withdrawn, the provisions of 35 U.S.C. 121 no longer apply. MPEP804.01. The examiner, however, maintains the restriction requirement regarding the sequences

The requirement is still deemed proper and is therefore made FINAL.

Priority

3. It is noted that this application appears to claim subject matter disclosed in prior Application No. 09/641,466, filed 08/18/2000. A reference to the prior application must be inserted as the first sentence(s) of the specification of this application or in an application data sheet (37 CFR 1.76), if applicant intends to rely on the filing date of the prior application under 35 U.S.C. 119(e), 120, 121, or 365(c). See 37 CFR 1.78(a). For benefit claims under 35 U.S.C. 120, 121, or 365(c), the reference must include the relationship (i.e., continuation, divisional, or continuation-in-part) of all nonprovisional applications. If the application is a utility or plant application filed under 35 U.S.C. 111(a) on or after November 29, 2000, the specific reference to the prior application

must be submitted during the pendency of the application and within the later of four months from the actual filing date of the application or sixteen months from the filing date of the prior application. If the application is a utility or plant application which entered the national stage from an international application filed on or after November 29, 2000, after compliance with 35 U.S.C. 371, the specific reference must be submitted during the pendency of the application and within the later of four months from the date on which the national stage commenced under 35 U.S.C. 371(b) or (f) or sixteen months from the filing date of the prior application. See 37 CFR 1.78(a)(2)(ii) and (a)(5)(ii). This time period is not extendable and a failure to submit the reference required by 35 U.S.C. 119(e) and/or 120, where applicable, within this time period is considered a waiver of any benefit of such prior application(s) under 35 U.S.C. 119(e), 120, 121 and 365(c). A benefit claim filed after the required time period may be accepted if it is accompanied by a grantable petition to accept an unintentionally delayed benefit claim under 35 U.S.C. 119(e), 120, 121 and 365(c). The petition must be accompanied by (1) the reference required by 35 U.S.C. 120 or 119(e) and 37 CFR 1.78(a)(2) or (a)(5) to the prior application (unless previously submitted), (2) a surcharge under 37 CFR 1.17(t), and (3) a statement that the entire delay between the date the claim was due under 37 CFR 1.78(a)(2) or (a)(5) and the date the claim was filed was unintentional. The Director may require additional information where there is a question whether the delay was unintentional. The petition should be addressed to: Mail Stop Petition, Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450.

If the reference to the prior application was previously submitted within the time period set forth in 37 CFR 1.78(a), but not in the first sentence(s) of the specification or an application data sheet (ADS) as required by 37 CFR 1.78(a) (e.g., if the reference was submitted in an oath or declaration or the application transmittal letter), and the information concerning the benefit claim was recognized by the Office as shown by its inclusion on the first filing receipt, the petition under 37 CFR 1.78(a) and the surcharge under 37 CFR 1.17(t) are not required. Applicant is still required to submit the reference in compliance with 37 CFR 1.78(a) by filing an amendment to the first sentence(s) of the specification or an ADS. See MPEP § 201.11.

It is noted that the statement for priority on page 1 of the specification was amended on July 24, 2003. However, the statement should indicate the U.S. patent number that was issued from the parent application.

Claim Objections

4. Applicant is advised that should claim 9 be found allowable, claim 14 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

5. Claim 3 is objected to because it contains non-elected subject matter.

6. Claim 12 is objected to because of the following informalities: the period punctuation mark is missing. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 1-19 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claims 1, 14 and 15: the recitation, "derived", renders the claim indefinite. The term suggests that the enhancer does not have to have the same sequence as the original enhancer of the virus. It is unclear what modifications are encompassed and how similar the sequences are between the "derived" enhancer and the original one. The metes and bounds are not clear. It is suggested that the recitation be removed from the claims.

In claim 10: it is unclear what is the resistance being provided to. Therefore, the metes and bounds are unclear.

8. Claims 1, 2, 4-19 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

A review of the full content of the specification indicates that an enhancer derived from a cassava vein mosaic virus is essential to the operation of the claimed invention. A review of the language of instant claims indicates that the claims are broadly drawn to any enhancer from a cassava vein mosaic virus. However, the specification only describes one of such enhancers, which is nucleotides 1 to 332 of SEQ ID NO: 1. Neither the specification nor the prior art describes any other enhancers from a cassava vein mosaic virus.

The Federal Circuit has recently clarified the application of the written description requirement. The court stated that a written description of an invention "requires a precise definition, such as by structure, formula, [or] chemical name, of the claimed subject matter sufficient to distinguish it from other materials." (See *University of California v. Eli Lilly and Co.*, 119 F.3d 1559, 1568; 43 USPQ2d 1398, 1406 (Fed. Cir. 1997)). The court also concluded that "naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a

description of that material." Id. Further, the court held that to adequately describe a claimed genus, Patent Owner must describe a representative number of the species of the claimed genus, and that one of skill in the art should be able to "visualize or recognize the identity of the members of the genus." Id.

Here, the specification does not correlate any other structure besides the enhancer of nucleotides 1-332 of SEQ ID NO: 1 with enhancer activity. Therefore, given the breadth of the claims and the lack of further guidance, a person skilled in the art would conclude that applicant does not provide adequate description of the whole claimed genus.

7. Claims 1-19 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the enhancer set forth by nucleotides 1-332 of SEQ ID NO: 1 with a formula $(X\text{-}Y)^2$ that functions together with promoter set forth by nucleotides 333-444 of SEQ ID NO: 1 in tobacco plant, it does not provide enablement for any enhancer from a cassava vein mosaic virus with a formula $(X\text{-}Y)^n$ (n is integer between 2 to 8) that functions together with any promoter in any organism. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make/use the invention commensurate in scope with these claims.

The instant claims are drawn to use an enhancer cassette with a formula $(X\text{-}Y)^n$ (n is integer between 2 to 8 and X is a enhancer domain from a cassava vein mosaic virus) that functions in any organism.

First, regarding claims 1-2, 4-19, neither the specification nor the prior art discloses any conserved structure(s) that constitute an enhancer from a cassava vein mosaic virus. The specification has not taught all enhancers from all CVMV strains. There is no evidence that the described enhancer of bases 1-332 of SEQ ID NO: 1 is the only enhancer in the genome of cassava vein mosaic virus. Sundaresan et al. (1995, *Genes Dev.* 9:1797:1810) and Comai et al. (1990, *Plant Mol. Biol.* 15:373-381) teach that it is only after extensive evaluation that promoters and enhancer elements have been identified for their enhanced performance in crop and tissue of interest (abstracts). Pennisi (2004, Science 306:632-635) also teaches that enhancers are especially hard to find because they are very small pieces of sequence and reside at varying distances from the gene they regulate (last paragraph in left column of page 633).Therefore, without further guidance, undue experimentation would be required for a person skilled in the art to identify all the potential enhancers in the genome of any and all cassava vein mosaic virus strains.

Regarding claims 2-3 and 19, the specification only teaches that a duplicated enhancer set forth by nucleotides 1-332 of SEQ ID NO: 1 functions in transgenic tobacco plants. However, the specification does not provide any evidence that formula other than $(X-Y)^2$ are expected to work similarly or better. Yu (US Patent Pub. No. 20030145357) teaches that if too many copies (e.g., more than 4 copies) of an enhancer are used, they may be spliced out from a vector through recombination when the vector is replicated in bacteria. In addition, too many copies of an enhancer may cause gene silencing in a transgenic plant (lines 6-10 in paragraph [0018]). Therefore,

although the promoter activity is increased proportionally to the copy number of an enhancer in general, the actual maximal copy number of an enhancer has to be determined by experimentation (lines 10-15 in paragraph [0018]).Taken together, in absence of further guidance, undue experimentation would be required for a person skilled in the art to determine the feasibility of using enhancers with the claimed formula in any organism.

Regarding claims 5 and 8-19, the specification teaches that the enhancer functions well together with the promoter set forth by nucleotides 333-444 of SEQ ID NO: 1. However, it is not enabled for all the promoters having an RNA polymerase binding site and an mRNA initiation site. Lewin (1983, Chapter 11: Promoters: the sites for initiating transcription, pages 174-194, in "Genes", New York: Wiley and Sons) teaches that the interaction of a viral enhancer with a cellular promoter may vary, because not all promoters are susceptible to enhancement. For example, the alpha globin gene promoter is not enhanced by the presence of the enhancer from SV40 (page 192, 1st paragraph on left col.). Given the unpredictability of the promoters that are susceptible to the claimed enhancers, undue experimentation would be required for a person skilled in the art to determine the promoters that can be used in the claimed invention.

Regarding claims 15-16 and 19, although the specification teaches that a duplicated enhancer set forth by nucleotides 1-332 of SEQ ID NO: 1 functions in transgenic tobacco plants, it is not enabled for all organisms. Pennisi also teaches that subtle variations in enhancers have had a big impact in development in two

echinoderms, the starfish and the sea urchin. A tiny change in the enhancer, which varies by just one binding site for a transcriptional factor, leads to a different transcriptional regulation of the gene (the paragraph bridging pages 634-635). The structurally conserved enhancer above could function differently in two closely related organisms. A person skilled in the art would not expect the claimed enhancer cassette would be active in non-plant cells. Therefore, given the unpredictability of the host cells suitable for the claimed enhancer, without further guidance, undue experimentation would be required for a person skilled in the art to determine the host range for the claimed enhancer.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to

consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

8. Claims 1-19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Verdaguer et al. (WO 97/48819) in view of McPherson et al. (U.S. Patent No. 5,164,316).

The instant claims are drawn to an enhancer cassette containing a duplicated enhancer from cassava vein mosaic virus (CsVMV), expression construct comprising such cassette, a promoter and a third nucleotide sequence of interest to be expressed, as well a GMO having such construct.

Verdaguer et al. teach expression vectors comprising CsVMV promoter sequence (including the enhancer element set forth by 1-332 of SEQ ID NO: 1 and the promoter set forth by nucleotides 333-444 of SEQ ID NO: 1) capable of initiating transcription of operably linked heterologous nucleotide sequence (page 4, lines 25-31 and page 5, lines 3-7) as well as the transgenic plant having the transformed vector (page 5, lines 8-10).

Verdaguer et al. do not teach duplicated enhancers.

McPherson et al. teach a vector comprising duplicated enhancer domains wherein the domains comprise a plurality of the repetitive units and the enhancer domain usually ranges from 25 bp – 1kb (see column 3, lines 1-68 and column 4, lines 3-7). McPherson et al. further teach that the vector construct have a transcription initiation region including a tandemly duplicated CaMV 35S enhancer sequence, a promoter comprising an RNA polymerase binding site and an mRNA initiation site, a

nucleotide sequence of interest and a termination region wherein all parts in the construct are operably linked (column 12, lines 66-68 and column 13, lines 1-6).

It would have been obvious to someone of ordinary skill in the art at the time of the instant invention to modify a vector taught by Verdaguer et al. with the duplicated enhancer structure as taught by McPherson et al., thus resulting in the practice of the instantly claimed invention with a reasonable expectation of success. One would have been motivated to do so given the teaching of Verdaguer et al. that the CsVMV promoter has a modular structure made of different domains that exert distinct influences on patterns of tissue specific expression and promoter expression requires synergistic or combinatorial interactions between different cis-element, which are reminiscent of CaMV 35S promoter (page 71, lines 10-16), and the teaching of McPherson et al. that duplicated enhancer elements of CaMV 35S gene can provide enhanced efficiency of transcription of the RNA coded region (column 2, lines 20-21) as well as the fact that enhancing transcription of gene of interest is highly desirable.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-7 an 9-19 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-3, 17-19 and 25-27 of U.S. Patent No. 6,664,384. Although the conflicting claims are not identical, they are not patentably distinct from each other because SEQ ID NO: 2 in the claim1 of U.S. Patent No. 6,664,384 comprising duplicated enhancer region of nucleotide 1-332 of SEQ ID NO: 1 as well as the promoter region of nucleotides 333-444 of SEQ ID NO: 1. Claims 2-3 of U.S. Patent No. 6,664,384 further teach the expression construct in which the enhancer cassette controls the expression of a gene encoding a disease or insect resistance protein or an antisense RNA. Furthermore, claim 17 of U.S. Patent No. 6,664,384 is directed to a cell comprising the expression cassette and the method of instant claim 19 was obviously carried out to make the cell. Therefore, claims 1-3, 17-19 and 25-27 of U.S. Patent No. 6,664,384 anticipate all the limitation set forth by instant claims 1-7 and 9-19.

Claim 8 is rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-3 of U.S. Patent No. 6,664,384 in view of Lewin (1983, Chapter 11: Promoters: the sites for initiating transcription, pages 174-194 in "Genes", New York: Wiley and Sons).

Claims 1-3 of U.S. Patent No. 6,664,384 teach duplicated enhancer region of nucleotide 1-332 of SEQ ID NO: 1 from cassava vein mosaic virus as well as the promoter region of nucleotides 333-444 of SEQ ID NO: 1.

Claims 1-3 of U.S. Patent No. 6,664,384 do not teach a heterologous promoter.

Lewin teaches that a viral enhancer can interact with various cellular promoter (page 192, 1st paragraph on left col.).

It would have been obvious for person with ordinary skill in the art to modify the claims 1-3 of U.S. Patent No. 6,664,384 to replace the nucleotides 333-444 of SEQ ID NO: 1 with a heterologous promoter according the teaching of Lewin et al, resulting in the claimed application with a reasonable expectation of success. One would have been motivated to do so given the teaching of Lewin that various cellular promoters interact with a viral enhancer (page 192, 1st paragraph on left col.).

Conclusion

Claims 1-19 are rejected.

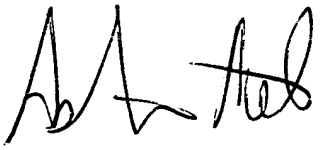
No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Li Zheng whose telephone number is 571-272-8031.

The examiner can normally be reached on Monday through Friday 9:00 AM - 5:30 PM EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anne Marie Grunberg can be reached on 571-272-0975. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



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PRIMARY EXAMINER